eunethta

EUROPEAN NETWORK FOR HEALTH TECHNOLOGY ASSESSMENT

D5.1 Submission Dossier – Table Template Collection – Medicinal Products

Version 1.0, 31/07/2023

Document history and contributors

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0.2	27-06-2023	Second draft
0.3	11-07-2023	Draft for CSCQ validation
0.4	26-07-2023	Endorsed by CEB
1.0	31-07-2023	Date of publication

Disclaimer

Participants

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The work in EUnetHTA 21 was a collaborative effort. While the agencies in the Hands-on Group actively wrote the deliverable, the entire EUnetHTA 21 consortium was involved in its production throughout various stages. This means that the Committee for Scientific Consistency and Quality (CSCQ) reviewed and discussed several drafts of the deliverable prior to validation. Afterwards the Consortium Executive Board (CEB) endorsed the final deliverable prior to publication.

Associated HTAb

The draft deliverable was reviewed by associated HTAb. The table template collection was not open for public consultation, as the draft guidance on the submission dossier template underwent public consultation between 04.07.2022 and 02.08.2022. Furthermore, a dedicated meeting was held with Health Technology Developers on July 13, 2023 to discuss the template.

Associated HTA bodies who reviewed	Dachverband der Österreichischen Sozialversicherung, [DVSV], Austria Norwegian Institute of Public Health, [NIPH], Norway Evaluation and Planning Unit – Directorate of the Canary Islands Health Service, [SESCS], Spain Regione Emilia-Romagna, [RER], Italy Health Information and Quality Authority [HIQA], Ireland DPA, Malta

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1 Results

1.1 Characterisation of included studies

Table 1: Characteristics of the included studies *[refers to table 19 in the submission dossier template]*

Study reference/ID	**Study type and design**	**Study population**	**Study arms (number of randomized/included patients)**	**Study duration, data cut off(s) and locations**	**Study endpoints**
<study 1>	*RCT,* *blind/open, parallel/cross-over, etc.*	*relevant characteristics, e.g. degree of severity including respective key inclusion/exclusion factors in footnotes*	*Group 1 (N = XX)* *Group 2 (N = XX)* *Group 3 (N = XX)*	• *Study duration:* • *Completion date (estimated, if study is ongoing): XX XX 20XX* • *1. Data cut-off: XX XX 20XX (planned interim analysis)* • *2. Data cut-off: XX XX 20XX (requested by EMA; not planned)* *(if complex can be described in separate paragraph)* • *Number of centres by continent*	*Primary:* *Key secondary[a]:* Other[b]: *(if complex can be described in separate paragraph)*
a: only secondary endpoints controlled for multiplicity b: only if included in at least one PICO					
N: number of included patients; RCT: randomized controlled trial;					

Table 2: Characterisation of the interventions of included studies *[refers to table 20 in the submission dossier template]*

Study reference/ID	**Study intervention**	**Study comparator**
Study XXX	*e.g. 250 µg, 1 Inhalation bid + Placebo 2 Inhalations bid*	*e.g.200 µg, 2 Inhalations bid + Placebo 1 Inhalation bid*
	<Optional additional content with treatment characteristics e.g. pre-treatment, treatment during the run-in phase, concomitant/prohibited medications as required>	
footnotes (please delete this line if it is not needed)		
abbreviations (please delete this line if it is not needed)		

1.2 Information on the course of included studies

1.2.1 For direct comparisons

Table 3: Information on the course of included studies - planned follow up times *[refers to table 21 in the submission dossier template]*

Study reference / ID Outcome category	**Planned follow-up**
<study 1>	
<outcome 1>	*<Until disease progression/x days after end of treatment, … >*
<outcome 2>	
<study 2>	
<outcome 1>	
<outcome 2>	
footnotes: (please delete this line, if it is not needed)	
abbreviations: (please delete this line, if it is not needed)	

1.2.2 For indirect comparisons

Table 4: Information on the course of included studies - planned follow up times *[refers to table 21 in the submission dossier template]*

Comparison **Study reference / ID** Outcome category	**Planned follow-up**
Intervention vs. (common) comparator	
<study 1>	
<outcome 1>	*<Until disease progression/x days after end of treatment, … >*
<outcome 2>	
<study 2>	
<outcome 1>	
<outcome 2>	
PICO comparator vs. (common) comparator	
<study 3>	
<outcome 1>	*<Until disease progression/x days after end of treatment, … >*
<outcome 2>	
<study 4>	
<outcome 1>	
<outcome 2>	
footnotes: (please delete this line, if it is not needed)	
abbreviations: (please delete this line, if it is not needed)	

1.3 Study results on relative effectiveness and relative safety

Table 5: Studies included in the assessment of patient population <X> per PICO question *[refers to table 22 in the submission dossier template]*

Study reference/ID **Relevant study arms (number of randomized/included patients)**	**Analysed population (number of randomized/included patients)**
PICO <X> *<type of comparison>: <XXX> vs. <YYY>*	
<study x> *<Group 1> (N = XX)* *<Group 2> (N = XX)*	*<characteristics x/y/z (if applicable)>* *Complete study population / relevant subpopulation[a]* *<Group 1> (n = XX)* *<Group 2> (n = XX)*
<study 1> *<Group 1> (N = XX)* *<Group 2> (N = XX)*	*Complete study population*
<study 2> *<Group 1> (N = XX)* *<Group 2> (N = XX)*	*<characteristics x/y/z>* *Relevant subpopulation[a]:* *<Group 1> (n = XX)* *<Group 2> (n = XX)*
PICO <X> *<type of comparison>: <XXX> vs. <YYY>*	
<study x> *<Group 1> (N = XX)* *<Group 2> (N = XX)*	*<characteristics x/y/z (if applicable)>* *Complete study population / relevant subpopulation[a]* *<Group 1> (n = XX)* *<Group 2> (n = XX)*
<study 1> *<Group 1> (N = XX)* *<Group 2> (N = XX)*	*Complete study population*
<study 2> *<Group 1> (N = XX)* *<Group 2> (N = XX)*	*<characteristics x/y/z>* *Relevant subpopulation[a]:* *<Group 1> (n = XX)* *<Group 2> (n = XX)*
a: In the case that a subpopulation of the study is analysed for the assessment, specify the number of included patients and describe the characteristics of the relevant subpopulation.	
N: number of randomized patients ; n: number of patients	

1.3.1 Patient characteristics

1.3.1.1 Table version for RCTs

Table 6: Patient baseline characteristics including treatment / study discontinuations for population <x> *[refers to table 23 in the submission dossier template]*

Study reference / ID **Characteristics** **Category**	**Study intervention**	**Relevant comparator**
<Study 1>	<intervention> N =	<comparator> N =
Age [years], mean (SD) Sex [f / m], % <more characteristics>, n (%) <Category 1> <Category 2> <Category 3> …		
Treatment discontinuation, n (%) Study discontinuation, n (%)		
<Study 2>	<intervention> N =	<comparator> N =
…		
footnotes (please delete this line if it is not needed)		
f: female; m: male; n: number of patients in the category, N: number of randomized patients; ND: no data;; RCT: randomized controlled trial; SD: standard deviation		

1.3.1.2 Table version for study types other than RCTs

Table 7 Patient baseline characteristics including treatment / study discontinuations for population <x> *[refers to table 23 in the submission dossier template]*

Study reference / ID **Characteristics** **Category**	**Study intervention**	**Relevant comparator**	**Standardized difference**
<Study 1>	<intervention> N =	<comparator> N =	
Age [years], mean (SD) Sex [f / m], % <more characteristics>, n (%) <Category 1> <Category 2> <Category 3> …			
Treatment discontinuation, n (%) Study discontinuation, n (%)			
<Study 2>	<intervention> N =	<comparator> N =	
…			
footnotes (please delete this line if it is not needed)			
f: female; m: male; n: number of patients in the category, N: number of randomized patients; ND: no data;; RCT: randomized controlled trial; SD: standard deviation			

1.3.2 Outcomes

1.3.2.1 For direct comparisons

Table 8: Matrix of outcomes in the included RCTs for PICO <x-1> - direct comparison: <intervention> vs. <PICO comparator> *[refers to table 24 in the submission dossier template]*

Outcomes	**Study reference/ID**		
	<study 1>	<study 2>	<study 3>
<outcome 1>, <OMI if applicable>	*<yes/no>*	*<yes/no>*	*<yes/no>*
<outcome 2>, <OMI if applicable>			
<outcome 3> , <OMI if applicable>			
<outcome 4> , <OMI if applicable>			
footnotes (please delete this line if it is not needed) OMI: Outcome Measurement Instrument			

Table 9: Information on the course of included studies – actual treatment duration and observation periods *[refers to table 25 in the submission dossier template]*

Study reference / ID Outcome category	**Study intervention**	**Relevant comparator**
<study 1> Treatment duration [<month/weeks>] Median [Min; Max] Mean (SD)	**<study intervention>** **N = / n^{x} =**	**<relevant comparator>** **N = / n^{x} =**
Observation period [<months/weeks>] <outcome> Median [Min; Max] Mean (SD) <outcome> Median [Min; Max] Mean (SD)		
<study 2> Treatment duration [<month/weeks>] Median [Min; Max] Mean (SD)	**<study intervention>** **N = / n^{x} =**	**<relevant comparator>** **N = / n^{x} =**
Observation period [<months/weeks>] <outcome> Median [Min; Max] Mean (SD) <outcome> Median [Min; Max] Mean (SD)		
x: if applicable: relevant subpopulation (<specify>)		
abbreviations: (please delete this line, if it is not needed)		

1.3.2.1.1 Effectiveness outcomes

Table 10: Relative effectiveness results (dichotomous outcomes) – direct comparison: <intervention> vs. <comparator> *[refers to table 26 in the submission dossier template]*

Time point	**<Intervention>**		**<Comparator>**		**<Intervention> vs. <Comparator>**			
Outcome Study reference/ID	**N**	**Patients with event n (%)**	**N**	**Patients with events n (%)**	**[e.g. RR] [95 %-CI] p-value**	**Hypothesis testing**	**RD [95 %-CI] p-value**	**Hypothesis testing**
<time point>								
<outcome 1> <study XXX> <study XXX>						<1> - <2> - <3>		
Total[x] (p_H = <XXX>; I^2 = <YYY>)								
<outcome 2> <study XXX> <study XXX>								
Total[x] (p_H = <XXX>; I^2 = <YYY>)								
Reading the "Hypothesis testing" columns: 1. Statistical significance: S = Satistically significant against the alpha level specified in the statistical analysis plan of the corresponding study, NS = Non-significant, NO = Nomimal p-value 2. Prespecification: P = Statistical test was prespecified according to the statistical analysis plan of the corresponding study, NP = Not prespecified 3. Multiple hypothesis testing. C = Appropriate control for multiplicity according to the statistical analysis plan and clinical study report of the corresponding study, NC = Not controlled								
x: calculated from meta-analysis								
CI: confidence interval, NI: No information, p_H: p-value from test for heterogeneity <specify>, RD: risk difference, RR. Relative risk								

Table 11: Relative effectiveness results (time to event outcomes) – direct comparison: <intervention> vs. <comparator> *[refers to table 26 in the submission dossier template]*

Time point Outcome Study reference/ID	**<Intervention>**		**<Comparator>**		**<Intervention> vs. <Comparator>**			
	N	**Median time to event in <weeks/months> [95 %-CI] patients with event n (%)**	**N**	**Median time to event in <weeks/months> [95 %-CI] patients with event n (%)**	**HR [95 %-CI] p-value**	**Hypothesis testing**	**<add appropriate absolute difference> p-value**	**Hypothesis testing**
<time point>								
Overall Survival								
<study XXX>						<1> - <2> - <3>		
<study XXX>								
Total[x] (p_H = <XXX>; I^2 = <YYY>)								
<outcome 2>								
<study XXX>								
<study XXX>								
Total[x] (p_H = <XXX>; I^2 = <YYY>)								

Reading the "Hypothesis testing" columns:
1. Statistical significance: S = Satistically significant against the alpha level specified in the statistical analysis plan of the corresponding study, NS = Non-significant, NO = Nomimal p-value
2. Prespecification: P = Statistical test was prespecified according to the statistical analysis plan of the corresponding study, NP = Not prespecified
3. Multiple hypothesis testing. C = Appropriate control for multiplicity according to the statistical analysis plan and clinical study report of the corresponding study, NC = Not controlled

x: calculated from meta-analysis

CI: confidence interval, HR: hazard ratio, NI: No information, p_H: p-value from test for heterogeneity <specify>

Table 12: Relative effectiveness results (quantitative outcomes) – direct comparison: <intervention> vs. <comparator> *[refers to table 26 in the submission dossier template]*

Time point	**<Intervention>**			**<Comparator>**			**<Intervention> vs. <Comparator>**	
Outcome Study reference/ID	**N**	**Values at baseline mean (SD)**	**Change/values at <time> mean] (SD)**	**N**	**Values at baseline mean (SD)**	**Change/values at <time> mean (SD)**	**<effect > [95 %-CI] p-value**	**Hypothesis testing**
<time point>								
<outcome 1>								
<study XXX>								<1> - <2> - <3>
<study XXX>								
Total[x] (p_H = <XXX>; I^2 = <YYY>)								
<outcome 2>								
<study XXX>								
<study XXX>								
Total[x] (p_H = <XXX>; I^2 = <YYY>)								

Reading the "Hypothesis testing" columns:
1. Statistical significance: S = Satistically significant against the alpha level specified in the statistical analysis plan of the corresponding study, NS = Non-significant, NO = Nomimal p-value
2. Prespecification: P = Statistical test was prespecified according to the statistical analysis plan of the corresponding study, NP = Not prespecified
3. Multiple hypothesis testing. C = Appropriate control for multiplicity according to the statistical analysis plan and clinical study report of the corresponding study, NC = Not controlled

x: calculated from meta-analysis

CI: confidence interval, NI: No information, p_H: p-value from test for heterogeneity <specify>, SD: standard deviation

1.3.2.1.2 Safety outcomes

Table 13: Safety outcomes including effect estimates (dichotomous outcomes) – direct comparison: <intervention> vs. <comparator> *[refers to table 27 in the submission dossier template]*

Time point	**<Intervention>**		**<Comparator>**		**<Intervention> vs. <Comparator>**	
Outcome Study reference/ID	**N**	**Patients with event n (%)**	**N**	**Patients with event n (%)**	**RR [95 %-CI]**	**RD [95 %-CI]**
<time point>						
At least one adverse event						
<study XXX>						
<study XXX>						
Total[a] (p_H = <XXX>; I^2 = <YYY>)						
Serious adverse events						
<study XXX>						
<study XXX>						
Total[a] (p_H = <XXX>; I^2 = <YYY>)						
Severe adverse events [insert used scale]						
<study XXX>						
Grade ≥ 3						
Grade 3						
Grade 4						
Grade 5						
<study XXX>						
Grade ≥ 3						
Grade 3						
Grade 4						
Grade 5						
Total[a] Grade ≥ 3 (p_H = <XXX>; I^2 = <YYY>)						
Treatment discontinuation due to adverse events						
<study XXX>						
<study XXX>						
Total[a] (p_H = <XXX>; I^2 = <YYY>)						

Time point	**<Intervention>**		**<Comparator>**		**<Intervention> vs. <Comparator>**	
Outcome Study reference/ID	**N**	**Patients with event n (%)**	**N**	**Patients with event n (%)**	**RR [95 %-CI]**	**RD [95 %-CI]**
Treatment interruption due to adverse events						
<study XXX>						
<study XXX>						
Total[a] (p_H = <XXX>; I^2 = <YYY>)						
Suspected unexpected serious adverse reaction						
<study XXX>						
<study XXX>						
Total[a] (p_H = <XXX>; I^2 = <YYY>)						
Specific adverse event A[b]						
<study XXX>						
<study XXX>						
Total[a] (p_H = <XXX>; I^2 = <YYY>)						
Specific adverse event B[b]						
<study XXX>						
<study XXX>						
Total[a] (p_H = <XXX>; I^2 = <YYY>)						

a: calculated from meta-analysis
b: As requested by member state(s) in their PICOs

AE: adverse event; N: number of randomized patients; n: number of patients with event; PICO: Population – Intervention – Comparator – Outcome; SAE: serious adverse event

Table 14: Safety outcomes (time to event outcomes) – direct comparison: <intervention> vs. <comparator> *[refers to table 27 in the submission dossier template]*

Time point	**<Intervention>**		**<Comparator>**		**<Intervention> vs. <Comparator>**	
Outcome Study reference/ID	**N**	**Median time to event in <weeks/months> [95 %-CI] patients with event n (%)**	**N**	**Median time to event in <weeks/months> [95 %-CI] patients with event n (%)**	**HR [95 %-CI] p-value**	**<add appropriate absolute difference> p-value**
<time point>						
At least one adverse event						
<study XXX>						
<study XXX>						
Total[a] (p_H = <XXX>; I^2 = <YYY>)						
Serious adverse events						
<study XXX>						
<study XXX>						
Total[a] (p_H = <XXX>; I^2 = <YYY>)						
Severe adverse events [insert used scale]						
<study XXX>						
Grade ≥ 3						
Grade 3						
Grade 4						
Grade 5						
<study XXX>						
Grade ≥ 3						
Grade 3						
Grade 4						
Grade 5						
Total[a] Grade ≥ 3 (p_H = <XXX>; I^2 = <YYY>)						

Time point	**<Intervention>**		**<Comparator>**		**<Intervention> vs. <Comparator>**	
Outcome Study reference/ID	**N**	**Median time to event in <weeks/months> [95 %-CI] patients with event n (%)**	**N**	**Median time to event in <weeks/months> [95 %-CI] patients with event n (%)**	**HR [95 %-CI] p-value**	**<add appropriate absolute difference> p-value**
Treatment discontinuation due to adverse events <study XXX> <study XXX> Total[a] (p_H = <XXX>; I^2 = <YYY>)						
Treatment interruption due to adverse events <study XXX> <study XXX> Total[a] (p_H = <XXX>; I^2 = <YYY>)						
Suspected unexpected serious adverse reaction <study XXX> <study XXX> Total[a] (p_H = <XXX>; I^2 = <YYY>)						
Specific adverse event A[b] <study XXX> <study XXX> Total[a] (p_H = <XXX>; I^2 = <YYY>)						
Specific adverse event B[b] <study XXX> <study XXX> Total[a] (p_H = <XXX>; I^2 = <YYY>)						
a: calculated from meta-analysis b: As requested by member state(s) in their PICOs						
AE: adverse event; N: number of randomized patients; n: number of patients with event; PICO: Population – Intervention – Comparator – Outcome; SAE: serious adverse event						

Table 15: Adverse events (all) by SOC and PT *[refers to table 28 in the submission dossier template]*

Time point **Study reference/ID** **Safety outcome** SOC PT	**<Intervention>** **N=**	**<Comparator>** **N=**	**<Intervention> vs. <comparator>**	
	Patients with event n (%)	**Patients with event n (%)**	**RR [95 %-CI]; p-value**	**RD [95 %-CI]; p-value**
<time point>				
Total AE				
System organ class A AE1 AE2				
System organ class B AE1 AE2				
System organ class C AE1 AE2				
footnotes (this line can be deleted if it is not needed) AE: adverse event, CI: Confidence interval; N: number of randomized patients; n: number of patients with event; PT: Preferred Term, RD: risk difference , RR: relative risk, SOC: System Organ Class				

Table 16: Adverse events (serious) by SOC and PT *[refers to table 28 in the submission dossier template]*

Time point **Study reference/ID** **Safety outcome** SOC PT	**<Intervention>** **N=**	**<Comparator>** **N=**	**<Intervention> vs. <comparator>**	
	Patients with event n (%)	**Patients with event n (%)**	**RR [95 %-CI]; p-value**	**RD [95 %-CI]; p-value**
<time point>				
Total SAE				
System organ class A SAE1 SAE2				
System organ class B SAE1 SAE2				
System organ class C SAE1 SAE2				
footnotes (this line can be deleted if it is not needed) CI: Confidence interval; N: number of randomized patients; n: number of patients with event; PT: preferred Term, RD: risk difference , RR: relative risk, SAE: serious adverse event, SOC: System Organ Class				

Table 17: Discontinuation due to adverse events by SOC and PT *[refers to table 28 in the submission dossier template]*

Time point **Study reference/ID** **Safety outcome** SOC PT	**<Intervention>** **N=** **Patients with event n (%)**	**<Comparator>** **N=** **Patients with event n (%)**	**<Intervention> vs. <comparator>** **RR [95 %-CI]; p-value**	**<Intervention> vs. <comparator>** **RD [95 %-CI]; p-value**
<time point>				
Total discontinuation due to AE				
System organ class A AE1 AE2				
System organ class B AE1 AE2				
System organ class C AE1 AE2				
footnotes (this line can be deleted if it is not needed) AE: adverse event, CI: Confidence interval; N: number of randomized patients; n: number of patients with event; PT: Preferred Term, RD: risk difference , RR: relative risk, SOC: System Organ Class				

1.3.2.1.3 Subgroup analyses

Table 18: Subgroup analyses (dichotomous outcomes) – direct comparison: <intervention> vs. <comparator> *[refers to table 29 in the submission dossier template]*

Time point	**<Intervention>**		**<Comparator>**		**<Intervention> vs. <Comparator>**			
Outcome Variable Study reference/ID subgroups	**N**	**Patients with event n (%)**	**N**	**Patients with events n (%)**	**[e.g. RR] [95 %-CI] p-value**	**Hypothesis testing**	**RD [95 %-CI] p-value**	**Hypothesis testing**
<time point>								
<outcome 1> <variable X> <study XXX> <subgroup 1> <subgroup 2> <study XXX> <subgroup 1> <subgroup 2>						<1> - <2> - <3>		<1> - <2> - <3>
Total[x] (p_H = <XXX>; I^2 = <YYY>) <subgroup 1> <subgroup 2>					Interaction[y]:		Interaction[y]:	
<outcome 2> *<to be displayed as above>*								

Reading the "Hypothesis testing" columns:
1. Statistical significance: S = Satistically significant against the alpha level specified in the statistical analysis plan of the corresponding study, NS = Non-significant, NO = Nomimal p-value
2. Prespecification: P = Statistical test was prespecified according to the statistical analysis plan of the corresponding study, NP = Not prespecified
3. Multiple hypothesis testing. C = Appropriate control for multiplicity according to the statistical analysis plan and clinical study report of the corresponding study, NC = Not controlled

x: calculated from meta-analysis
y: <specify>

CI: confidence interval, NI: No information, p_H: p-value from test for heterogeneity <specify>, RD: risk difference, RR. Relative risk

Table 19: subgroup analyses (time to event outcomes) – direct comparison: <intervention> vs. <comparator *[refers to table 29 in the submission dossier template]*

Time point	**<Intervention>**		**<Comparator>**		**<Intervention> vs. <Comparator>**			
Outcome Variable Study reference/ID subgroups	**N**	**Median time to event in <weeks/months> [95 %-CI] patients with event n (%)**	**N**	**Median time to event in <weeks/months> [95 %-CI] patients with event n (%)**	**HR [95 %-CI] p-values**	**Hypothesis testing**	**<add appropriate absolute difference> p-value**	**Hypothesis testing**
<time point>								
<outcome 1> <variable X> <study XXX> <subgroup 1> <subgroup 2> <study XXX> <subgroup 1> <subgroup 2>						<1> - <2> - <3>		<1> - <2> - <3>
Total[x] (p_H = <XXX>; I^2 = <YYY>) <subgroup 1> <subgroup 2>					Interaction[y]:		Interaction[y]:	
<outcome 2> *<to be displayed as above>*								
Reading the "Hypothesis testing" columns: 1. Statistical significance: S = Satistically significant against the alpha level specified in the statistical analysis plan of the corresponding study, NS = Non-significant, NO = Nomimal p-value 2. Prespecification: P = Statistical test was prespecified according to the statistical analysis plan of the corresponding study, NP = Not prespecified 3. Multiple hypothesis testing. C = Appropriate control for multiplicity according to the statistical analysis plan and clinical study report of the corresponding study, NC = Not controlled								
x: calculated from meta-analysis y_ <specify>								
CI: confidence interval, HR: hazard ratio, NI: No information, p_H: p-value from test for heterogeneity <specify>								

Table 20: subgroup analyses (quantitative outcomes) – direct comparison: <intervention> vs. <comparator> *[refers to table 29 in the submission dossier template]*

Time point	**<Intervention>**			**<Comparator>**			**<Intervention> vs. <Comparator>**	
Outcome Variable Study reference/ID subgroups	**N**	**Values at baseline mean (SD)**	**Change/values at <time> mean] (SD)**	**N**	**Values at baseline mean (SD)**	**Change/values at <time> mean (SD)**	**<effect > [95 %-CI] p-value**	**Hypothesis testing**
<time point>								
<outcome 1> <variable X> <study XXX> <subgroup 1> <subgroup 1> <study XXX> <subgroup 1> <subgroup 1>								<1> - <2> - <3>
Total[x] (p_H = <XXX>; I^2 = <YYY>) <subgroup 1> <subgroup 1>							Interaction[y]:	
<outcome 2> *<to be displayed as above>*								

Reading the "Hypothesis testing" columns:
1. Statistical significance: S = Satistically significant against the alpha level specified in the statistical analysis plan of the corresponding study, NS = Non-significant, NO = Nomimal p-value
2. Prespecification: P = Statistical test was prespecified according to the statistical analysis plan of the corresponding study, NP = Not prespecified
3. Multiple hypothesis testing. C = Appropriate control for multiplicity according to the statistical analysis plan and clinical study report of the corresponding study, NC = Not controlled

x: calculated from meta-analysis
y: <specify>

CI: confidence interval, NI: No information, p_H: p-value from test for heterogeneity <specify>, SD: standard deviation

1.3.2.2 For indirect comparisons

Table 21: Matrix of outcomes in the included studies for PICO <x-1> - indirect comparison: <intervention> vs. <PICO comparator> *[refers to table 24 in the submission dossier template]*

Outcomes	**Comparison Study reference/ID**				**Indirect comparison method**
	<intervention> vs. <common comparator>		**<PICO comparator> vs. <common comparator>**		
	<study 1>	<study 2>	<study 3>	<study 4>	
<outcome 1>, <OMI if applicable>	*<yes/no>*	*<yes/no>*	*<yes/no>*	*<yes/no>*	*e.g. Bucher ITC, NMA, MAIC (anchored/unanchored), N/A*
<outcome 2>, <OMI if applicable>					
<outcome 3>, <OMI if applicable>					
<outcome 4>, <OMI if applicable>					
footnotes (please delete this line if it is not needed) OMI: outcome measure instrument					

Table 22: Information on the course of included studies – actual treatment duration and observation periods
[refers to table 25 in the submission dossier template]

Comparison **Study reference / ID** Outcome category	**Study intervention**	**Relevant comparator**
Intervention vs. (common) comparator		
<study 1> Treatment duration [<month/weeks>] Median [Min; Max] Mean (SD)	**<study intervention>** **N = / n^{x} =**	**<relevant comparator>** **N = / n^{x} =**
Observation period [<months/weeks>] <outcome> Median [Min; Max] Mean (SD) <outcome> Median [Min; Max] Mean (SD)		
<study 2> Treatment duration [<month/weeks>] Median [Min; Max] Mean (SD)	**<study intervention>** **N = / n^{x} =**	**<relevant comparator>** **N = / n^{x} =**
Observation period [<months/weeks>] <outcome> Median [Min; Max] Mean (SD) <outcome> Median [Min; Max] Mean (SD)		
PICO comparator vs. (common) comparator		
<study 3> Treatment duration [<month/weeks>] Median [Min; Max] Mean (SD)	**<study intervention>** **N = / n^{x} =**	**<relevant comparator>** **N = / n^{x} =**
Observation period [<months/weeks>] <outcome> Median [Min; Max] Mean (SD) <outcome> Median [Min; Max] Mean (SD)		
<study 4> Treatment duration [<month/weeks>] Median [Min; Max] Mean (SD)	**<study intervention>** **N = / n^{x} =**	**<relevant comparator>** **N = / n^{x} =**
Observation period [<months/weeks>] <outcome> Median [Min; Max] Mean (SD) <outcome> Median [Min; Max] Mean (SD)		
x: if applicable: relevant subpopulation (<specify>)		
abbreviations: (please delete this line, if it is not needed)		

1.3.2.2.1 Effectiveness outcomes

Table 23: Relative effectiveness results (dichotomous outcomes) – indirect comparison: <intervention> vs. <comparator> *[refers to table 26 in the submission dossier template]*

Time point Outcome Study reference/ID	**<Intervention> / <PICO comparator>**		**<(Common) comparator>**		**Group difference**			
	N	**Patients with event n (%)**	**N**	**Patients with events n (%)**	**[e.g. RR] [95 %-CI] p-value**	**Hypothesis testing**	**RD [95 %-CI] p-value**	**Hypothesis testing**
<time point>								
<outcome 1>								
<intervention> vs. <(common) comparator>								
<study XXX>						<1> - <2> - <3>		
<study XXX>								
Total[x] (p_H = <XXX>; I^2 = <YYY>)								
<PICO comparator> vs. <(common) comparator>								
<study XXX>						<1> - <2> - <3>		
<study XXX>								
Total[x] (p_H = <XXX>; I^2 = <YYY>)								
Indirect comparison (<method used (e.g. Bucher, MAIC etc)>): <intervention> vs. <PICO comparator>								

Time point Outcome Study reference/ID	**<Intervention> / <PICO comparator>**		**<(Common) comparator>**		**Group difference**			
	N	**Patients with event n (%)**	**N**	**Patients with events n (%)**	**[e.g. RR] [95 %-CI] p-value**	**Hypothesis testing**	**RD [95 %-CI] p-value**	**Hypothesis testing**
<outcome 2> *<to be displayed as above>*								
Reading the "Hypothesis testing" columns: 1. Statistical significance: S = Satistically significant against the alpha level specified in the statistical analysis plan of the corresponding study, NS = Non-significant, NO = Nomimal p-value 2. Prespecification: P = Statistical test was prespecified according to the statistical analysis plan of the corresponding study, NP = Not prespecified 3. Multiple hypothesis testing. C = Appropriate control for multiplicity according to the statistical analysis plan and clinical study report of the corresponding study, NC = Not controlled								
x: calculated from meta-analysis								
CI: confidence interval, NI: No information, p_H: p-value from test for heterogeneity <specify>, RD: risk difference, RR. Relative risk								

Table 24: Relative effectiveness results (time to event outcomes) – indirect comparison: <intervention> vs. <comparator> *[refers to table 26 in the submission dossier template]*

Time point Outcome Study reference/ID	**<Intervention> / <PICO comparator>**		**<(Common) comparator>**		**Group difference**			
	N	**Median time to event in <weeks/months> [95 %-CI] patients with event n (%)**	**N**	**Median time to event in <weeks/months> [95 %-CI] patients with event n (%)**	**HR [95 %-CI] p-value**	**Hypothesis testing**	**<add appropriate absolute difference> p-value**	**Hypothesis testing**
<time point>								
<outcome 1>								
<intervention> vs. <(common) comparator>								
<study XXX>						<1> - <2> - <3>		
<study XXX>								
Total[x] (p_H = <XXX>; I^2 = <YYY>)								
<PICO comparator> vs. <(common) comparator>								
<study XXX>						<1> - <2> - <3>		
<study XXX>								
Total[x] (p_H = <XXX>; I^2 = <YYY>)								
Indirect comparison (<method used (e.g. Bucher, MAIC etc)>): <intervention> vs. <PICO comparator>								

Time point Outcome Study reference/ID	**<Intervention> / <PICO comparator>**		**<(Common) comparator>**		**Group difference**			
	N	**Median time to event in <weeks/months> [95 %-CI] patients with event n (%)**	**N**	**Median time to event in <weeks/months> [95 %-CI] patients with event n (%)**	**HR [95 %-CI] p-value**	**Hypothesis testing**	**<add appropriate absolute difference> p-value**	**Hypothesis testing**
<outcome 2> *<to be displayed as above>*								
Reading the "Hypothesis testing" columns: 1. Statistical significance: S = Satistically significant against the alpha level specified in the statistical analysis plan of the corresponding study, NS = Non-significant, NO = Nomimal p-value 2. Prespecification: P = Statistical test was prespecified according to the statistical analysis plan of the corresponding study, NP = Not prespecified 3. Multiple hypothesis testing. C = Appropriate control for multiplicity according to the statistical analysis plan and clinical study report of the corresponding study, NC = Not controlled								
x: calculated from meta-analysis								
CI: confidence interval, NI: No information, p_H: p-value from test for heterogeneity <specify>, RD: risk difference, RR. Relative risk								

Table 25: Relative effectiveness results (quantitative outcomes) – indirect comparison : <intervention> vs. <comparator> *[refers to table 26 in the submission dossier template]*

Time point Outcome Study reference/ID	**<Intervention> / <PICO comparator>**			**<(Common) comparator>**			**Group difference**	
	N	**Values at baseline mean (SD)**	**Change/values at <time> mean] (SD)**	**N**	**Values at baseline mean (SD)**	**Change/values at <time> mean] (SD)**	**<effect> [95 %-CI] p-value**	**Hypothesis testing**
<time point>								
<outcome 1>								
<intervention> vs. <(common) comparator>								
<study XXX>								<1> - <2> - <3>
<study XXX>								
Total[x] (p_H = <XXX>; I^2 = <YYY>)								
<PICO comparator> vs. <(common) comparator>								
<study XXX>								<1> - <2> - <3>
<study XXX>								
Total[x] (p_H = <XXX>; I^2 = <YYY>)								
Indirect comparison (<method used (e.g. Bucher, MAIC etc)>): <intervention> vs. <PICO comparator>								

Time point Outcome Study reference/ID	**<Intervention> / <PICO comparator>**			**<(Common) comparator>**			**Group difference**	
	N	**Values at baseline mean (SD)**	**Change/values at <time> mean] (SD)**	**N**	**Values at baseline mean (SD)**	**Change/values at <time> mean] (SD)**	**<effect> [95 %-CI] p-value**	**Hypothesis testing**
<outcome 2> *<to be displayed as above>*								
Reading the "Hypothesis testing" columns: 1. Statistical significance: S = Satistically significant against the alpha level specified in the statistical analysis plan of the corresponding study, NS = Non-significant, NO = Nomimal p-value 2. Prespecification: P = Statistical test was prespecified according to the statistical analysis plan of the corresponding study, NP = Not prespecified 3. Multiple hypothesis testing. C = Appropriate control for multiplicity according to the statistical analysis plan and clinical study report of the corresponding study, NC = Not controlled								
x: calculated from meta-analysis								
CI: confidence interval, NI: No information, p_H: p-value from test for heterogeneity <specify>, RD: risk difference, RR. Relative risk								

1.3.2.2.2 Safety outcomes

Table 26: Safety outcomes including effect estimates (dichotomous outcomes) – indirect comparison: <intervention> vs. <comparator> *[refers to table 27 in the submission dossier template]*

Time point Outcome Study reference/ID	**<Intervention> / <PICO comparator>**		**<(Common) comparator>**		**Group difference**	
	N	**Patients with event n (%)**	**N**	**Patients with event n (%)**	**RR [95 %-CI]**	**RD [95 %-CI]**
<time point>						
At least one adverse event						
<intervention> vs. <(common) comparator>						
<study XXX>						
<study XXX>						
Total[a] (p_H = <XXX>; I^2 = <YYY>)						
<PICO comparator> vs. <(common) comparator>						
<study XXX>						
<study XXX>						
Total[a] (p_H = <XXX>; I^2 = <YYY>)						
Indirect comparison (<method used (e.g. Bucher, MAIC etc)>): <intervention> vs. <PICO comparator>						
Serious adverse events						
<to be displayed as above>						
Severe adverse events [insert used scale]						
<to be displayed as above>						
Treatment discontinuation due to adverse events						
<to be displayed as above>						

Time point Outcome Study reference/ID	**<Intervention> / <PICO comparator>**		**<(Common) comparator>**		**Group difference**	
	N	**Patients with event n (%)**	**N**	**Patients with event n (%)**	**RR [95 %-CI]**	**RD [95 %-CI]**
Treatment interruption due to adverse events *<to be displayed as above>*						
Suspected unexpected serious adverse reaction *<to be displayed as above>*						
Specific adverse event A[b] *<to be displayed as above>*						
Specific adverse event B[b] *<to be displayed as above>*						
a: calculated from meta-analysis b: As requested by member state(s) in their PICOs						
AE: adverse event; N: number of randomized patients; n: number of patients with event; PICO: Population – Intervention – Comparator – Outcome; SAE: serious adverse event						

Table 27: Safety outcomes including effect estimates (time to event outcomes) – indirect comparison: <intervention> vs. <comparator> *[refers to table 27 in the submission dossier template]*

Time point Outcome Study reference/ID	**<Intervention> / <PICO comparator>**		**<(Common) comparator>**		**Group difference**	
	N	**Median time to event in <weeks/months> [95 %-CI] patients with event n (%)**	**N**	**Median time to event in <weeks/months> [95 %-CI] patients with event n (%)**	**HR [95 %-CI]**	**<add appropriate absolute difference> p-value**
<time point>						
At least one adverse event						
<intervention> vs. <(common) comparator>						
<study XXX>						
<study XXX>						
Total[a] (p_H = <XXX>; I^2 = <YYY>)						
<PICO comparator> vs. <(common) comparator>						
<study XXX>						
<study XXX>						
Total[a] (p_H = <XXX>; I^2 = <YYY>)						
Indirect comparison (<method used (e.g. Bucher, MAIC etc)>): <intervention> vs. <PICO comparator>						
Serious adverse events *<to be displayed as above>*						
Severe adverse events [insert used scale] *<to be displayed as above>*						
Treatment discontinuation due to adverse events *<to be displayed as above>*						

Time point Outcome Study reference/ID	**<Intervention> / <PICO comparator>**		**<(Common) comparator>**		**Group difference**	
	N	**Median time to event in <weeks/months> [95 %-CI] patients with event n (%)**	**N**	**Median time to event in <weeks/months> [95 %-CI] patients with event n (%)**	**HR [95 %-CI]**	**<add appropriate absolute difference> p-value**
Treatment interruption due to adverse events *<to be displayed as above>*						
Suspected unexpected serious adverse reaction *<to be displayed as above>*						
Specific adverse event A[b] *<to be displayed as above>*						
Specific adverse event B[b] *<to be displayed as above>*						
a: calculated from meta-analysis b: As requested by member state(s) in their PICOs						
AE: adverse event; N: number of randomized patients; n: number of patients with event; PICO: Population – Intervention – Comparator – Outcome; SAE: serious adverse event						